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## Fax/Mail

Dear Sirs

**RE: Patent Application No. PCT/GB2004/002021 in International (PCT)  
in the name of Oxitec Limited**

The International Search Examiner considers that the only relevant citation is D1 (Nature Biotechnology). This document discloses refugia. The present application also discusses refugia, but we respectfully submit that, in the context of diluting and eliminating resistance, the Examiner may have misunderstood the present invention.

The whole point of the present application is to dilute resistance in a population by the direct introduction of a wild type individual into a population having the resistant trait. On the other hand, the refugia of D1 are specifically there to provide a refuge for non-resistant insects in order to discourage too much resistance development.

In fact, as we have already pointed out, the provision of refugia, even in large quantities, cannot prevent the eventual prevalence of large amounts of resistance.

By contrast, if the wild type, non-resistant trait is introduced in the homozygous form back into the population, directly, rather than being simply encouraged by the existence of refugia, then this actually serves to substantially reduce and even eliminate resistance, in direct contrast to what can be achieved simply using refugia.

Put in another way, refugia simply permit the continued existence of non-resistant individuals, but do nothing to re-establish the wild type, whereas direct reintroduction of the wild type encourages dilution and extinction of resistance. The Examiner may have possibly also confused herself with our use of refugia to help with the process, but we stress that it is important not to confuse the use of refugia and RIDL with the primary concept behind the present invention.

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We request that this letter is retained on file and transmitted to the national/regional offices in due course. In the event that a Demand is filed, we also request that this letter is considered by the IPEA.

Yours sincerely,



H D LORD